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NEWS

RESIST – Resolving Infection Susceptibility

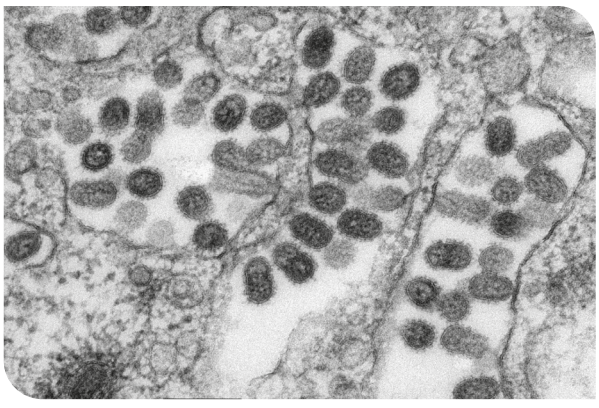
RESIST

Bird flu – a growing concern?

A STRAIN OF AVIAN FLU HAS SPREAD AROUND THE WORLD AND IS CAUSING HAVOC AMONG WILD BIRDS AND FARMED POULTRY, INFECTING MAMMALS AND KILLING COLONIES OF SEA LIONS. SHOULD WE BE CONCERNED ABOUT A POSSIBLE HUMAN OUTBREAK?

In the wake of the ongoing COVID-19 pandemic, the largest ever recorded outbreak of bird flu has featured dominantly in the news since it was first detected in late 2020, killing hundreds of millions of seabirds and poultry. Worryingly, it has since also spilled over into mammals and has been detected amongst others in foxes, bears, otters, raccoons and mink, even killing large populations of seals and sea lions. Alarmingly, an eleven-year-old girl in Cambodia died from bird flu in February, prompting concern of animal-to-human transmission.

Highly pathogenic bird flu is caused by highly pathogenic avian influenza A viruses (HPAIV) and is highly lethal to aquatic birds and farmed poultry. HPAIV is a different strain of the same virus that causes seasonal epidemics and occasional pandemics of influenza in humans. While HPAIV is highly lethal in humans, causing case-fatality rates of over 50 per cent, it is only very rarely able to infect humans and even more rarely able to be transmitted between humans.



Transmission electron microscope image of the influenza A(H5N1) virus, the causative agent of avian influenza.

This is due to a number of species barriers that HPAIV needs to overcome by adaptive mutations, most notably in its surface glycoprotein HA and its heterotrimeric RNA-dependent RNA polymerase (PB2, PB1, PA). These adaptive mutations enable an avian influenza A virus to preferentially bind to the human binding receptor for influenza A virus entry, facilitate proteolytic cleavage of HA required for viral infection in a wide range of tissues and enable the viral polymerase to utilize mammalian instead of avian host factors needed for viral replication. Experimental studies have however shown, that with only a few mutations an avian adapted virus is able to efficiently infect ferrets and spread by aerosol transmission.

While the previous outbreaks of bird flu were mostly restricted to the Far East, especially China, Vietnam and Indonesia, the current bird flu outbreak has now spread to all continents with the exception of Australia and Antarctica. This can be explained by a subtle change in the nature of this current clade of HPAIV that delays disease in migratory aquatic birds, allowing the virus to spread further and faster along bird migration routes. This has also led to the dramatic increase in HPAIV cases in non-human mammals, mostly in species that hunt or scavenge on aqua- »

We

are pleased to present our new newsletter and offer you an informative article on the topic of avian flu starting on page 1. We also invite you to get to know new members of our cluster (page 3) and to learn about the projects and successes of our researchers (page 4). You will also find current news and dates (page 10) and you can find out how our science is brought closer to the public (from page 11). We hope you enjoy reading this spring issue.

Your RESIST spokesperson team

The RESIST speaker team: Prof. Schulz, Prof. Hansen and Prof. Förster (from left).

» tic birds. Worryingly, transmission between seals and sea lions has been observed, and in an outbreak in a Spanish mink farm, at least two mutations associated with mammalian adaptation were found in the virus, prompting concern of imminent human adaptation of HPAIV.

Compared to the early 2000s when H5N1 bird flu was causing hundreds of human deaths, so far only 4 recorded human cases and no fatalities have been found. The recent fatal Cambodian case of bird flu was found to have originated from an unrelated virus strain (H5N1 clade 2.3.2.1c) to the bird flu strain currently found all over the world (H5N1 clade 2.3.4.4b). While it is possible for HPAIV to gain the necessary mutations for mammalian adaptation in seals or minks, for a human pandemic to occur, zoonotic transmission from animals to humans still needs to take place first, which still is a relatively rare event. However, as the current outbreak of bird flu is not likely to go away anytime soon, more HPAIV will be circulating in birds and mammals, resulting in higher potential exposure rates for humans, providing ample opportunity for a single zoonotic introduction of a mammalian adapted virus into the human population.

Dr. Benjamin Nilsson-Payant

New members of the SAB

Prof. Notarangelo

Prof. Macpherson

Prof. Dr. Andrew J. Macpherson, Clinic for Gastroenterology, University Department of Visceral Surgery and Medicine, Inselspital, Bern, Switzerland, and Prof. Dr. Luigi Daniele Notarangelo, National Institute of Allergy and Infectious Diseases (NIAID), Immune deficiency genetics diseases section, National Institutes of Health (NIH), Bethesda (Maryland), USA, have joined the RESIST Scientific Advisory Board in mid-March. Prof. Dr. Sandra Pellegrini, Institut Pasteur, Paris, France, retired from this board in July 2022.

Prof. Pellegrini

Dr. Carina Jürgens and Marie Schulze can be seen in the back row at places 3 and 4 (from left).

Deputies elected

Dr. Carina Jürgens and Marie Schulze have represented the interests of (post-) doctoral students in RESIST since mid-December 2022. Dr. Jürgens conducts research at the MHH Clinic for Gastroenterology, Hepatology, Infectious Diseases and Endocrinology; she has already represented doctoral students in RESIST since January 2020. Marie Schulze is currently doing her doctorate at the MHH Institute of Virology. Both want to ensure that the young scientists can establish good contacts among themselves. To this end, they have already organised well-attended regulars' meetings supported by RESIST in January and March, for example a sociable bowling evening, which will continue to take place every second month on the last Thursday. Contact: juergens.carina@mh-hannover.de, schulze.marie-sophie@mh-hannover.de.

Welcome to RESIST

PROF. SLEVOGT, PROF. SÜHS AND DR. RÖSNER ARE NEW MEMBERS OF RESIST

Prof. Dr. Hortense Slevogt, a renowned expert in infectious diseases of the respiratory tract, joined the RESIST team in mid-November 2022: She is a new member and also serves on the RESIST Internal Advisory Board (IAB).

She studied medicine in Berlin and worked as a physician and scientist for 17 years in the Medical Clinic with a focus on infectiology and pneumology at the Charité in Berlin. In 2011, she moved to the University Hospital of Jena, where she led a research group, and since 2017 she has also worked in the Clinic for Internal Medicine I. Prof. Slevogt came to MHH in 2022, and she is a senior consultant in the Clinic for Pneumology and Infectiology. Her area of responsibility includes the diagnosis and therapy of people with infections of the respiratory tract, with infections in immunosuppression or with tropical medical infections.

At the HZI in Braunschweig, she heads the research group "Dynamics of respiratory infections". Her research laboratory is located there, which further strengthens translational research between the MHH and the HZI. She researches the importance of the lung microbiome for inflammation of the respiratory tract and analyses the role of commensals – microorganisms in the airways and lungs that do not cause infections – as a component of the lung microbiome. "I am interested in the importance of commensals in relation to susceptibility to respiratory infections and their influence on the pulmonary immune response and thus on the course of lung infections," she says.

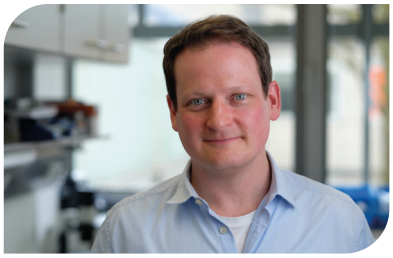
As part of RESIST, Prof. Slevogt is investigating the interactions between commensals and microbial pathogens and the influence of this interaction on the shaping of the immunological milieu in the airways and lungs. Among other things, she analyses the effects of the direct interaction of bacterial commensals of the lung microbiome of healthy individuals on the epithelium of the airways and she characterises these effects on infections of the airway epithelium with bacterial lung pathogens.

Prof. Dr. Kurt-Wolfram Sühs, senior physician in the MHH Department of Neurology with Clinical Neurophysiology, is focusing his research in RESIST with his research team on the varicella-zoster virus (VZV), which can cause shingles when reactivated. "We want to find out which factors lead to a severe course of the disease in this case," says the neurologist.

To this end, he is investigating clinical and genetic factors as well as biomarkers in the cerebrospinal fluid of patients suffering from VZV. "This information will provide clues for a better understanding of the disease and for clinical treatment, and may form the basis for identifying new targets for the treatment of severe courses of VZV infection," he describes. Prof. Sühs is involved in the RESIST research projects A3 and A4.

The focus of his working group is also research on neuroimmunological mechanisms in inflammatory diseases of the nervous system, especially autoimmune and infectious encephalitides. He is interested in which mechanisms underlie these diseases, which factors influence the diseases and their severity and whether these influences can be used for diagnostics, individual prognosis assessment and therapy.

Prof. Sühs studied and did his doctorate at the MHH, and was an assistant physician in neurology at the University of Göttingen and Saarland University, Homburg. He joined the MHH Department of Neurology in 2012 and became a senior physician in 2017. He was appointed professor in 2022.



Dr. Lennart Rösner is dedicated to atopic dermatitis, which begins with a defect in the skin barrier in interaction with changes in the immune system. The triggers for a worsening of this chronic inflammatory and agonisingly itchy skin disease can be allergens, skin irritating substances, mechanical stimuli, psychological stress as well as bacterial infections, and some affected persons have an increased susceptibility to viral diseases.

In order to be able to help them in the long term, Dr. Rösner is exploring the cellular immune response to *Staphylococcus aureus* bacteria and herpes viruses as part of RESIST. "My research aims at an in-depth characterisation of specific T cells to assess their impact on infection of the skin and other organs. I am also investigating factors in the skin of these patients that could favour infection," explains the researcher from the MHH Department of Dermatology, Allergology and Venerology.

In addition, Dr. Rösner is involved in leading the RESIST cohort of elderly people. "With it, we are investigating the ageing of the immune system and the associated increased risk of suffering from various infectious diseases in old age," he says. Dr. Rösner is also involved in the RESIST research projects A3, A4, B5 and B12.

Breaking resistance and inhibiting herpes

Prof. Hirsch

PROF. HIRSCH AWARDED ERC PROOF OF CONCEPT GRANT

Prof. Hirsch has received an ERC Proof of Concept Grant from the European Research Council (ERC). For her, this means financial support for the search for new antibiotics against resistant bacteria as well as a very valuable recognition of her work to date. This award can only be given to someone who has made very good progress with their work within the framework of an ERC Starting Grant – which she was able to acquire in 2018.

Prof. Hirsch is head of the Drug Design and Optimization Department at the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), a professor at Saarland University, a scientist at the German Center for Infection Research (DZIF) and on the leadership team of the RESIST project D1. HIPS is a site of the Helmholtz Centre for Infection Research (HZI) in collaboration with Saarland University.

As part of her ERC Starting Grant, she succeeded in identifying novel molecules that attack a previously unused target structure in bacteria and are thus a promising starting point for the development of resistance-breaking antibiotics. One of the target structures, also called "targets", is a protein called DnaN. It is responsible for the repair and production of new DNA. If DnaN is switched off by active substances, the affected bacteria can no longer reproduce. This makes DnaN an extremely attractive target for the development of new drugs.

The ERC Proof of Concept funding of 150,000 euros that has now been obtained will give Prof. Hirsch the opportunity to further optimise her most promising drug candidate – with the aim of finding a preclinical candidate and thus progressing towards a possible application.

The search for new active agents against antibiotic-resistant bacteria could also open up new therapeutic options for herpesvirus diseases: In the RESIST project D1, of which Prof. Hirsch is also a member of the leadership team, the aim is to prevent herpes viruses from multiplying and persisting in the body. Here, too, the researchers are looking for target structures for inhibitory agents. "One target of herpes viruses, pORF59, is the viral counterpart to the DnaN of bacteria, they are structurally similar. If we can find compounds that can knock out DnaN, we will also have more knowledge about compounds that can inhibit pORF59 and thus target herpes viruses," she explains.

Freedom for innovation

REPAIRING TISSUES AND ORGANS: NEW TRAINING PROGRAMME NEXTGENERATION

Prof. Lachmann, Prof. Happle and Dr. Zweigerdt (from left) present the importance of networking science and medicine.

On 1 July, the new training programme nextGENERATION on regenerative medicine for young scientists with doctorates will start at the MHH. "One of the main goals of nextGENERATION is to translate regenerative concepts into advanced therapies for patients. To do this, we use cutting-edge technologies of regenerative medicine to repair tissues and organs, such as stem cell-based therapies and gene therapies," describes RESIST Prof. Dr. Nico Lachmann, spokesperson of the new programme, which is funded by the Else Kröner-Fresenius-Stiftung (EKFS) with one million euros. The participants will carry out innovative projects with these cutting-edge technologies, but they will also learn more about the demands of patient care and further their careers through independent work. The three-year programme is designed for six researchers who have completed their doctorate between one and four years ago.

They are individually supervised in the implementation of their research projects and participate in tailor-made medical lectures as well as translational seminars and further training. They will also be able to enhance their project management skills and advance their careers individually. "The programme will enable them to take on leading positions in regenerative research and seamlessly connect between universities, clinics and industry," says Dr. Robert Zweigerdt, co-spokesperson of the programme. The networking of young, excellent scientists with clinical questions and problems is of particular importance, he says, because this is the only way new therapies make it to the clinic and thus to the patients. "We have set ourselves the goal of giving bright young minds the freedom to develop medical innovations, while at the same time providing the tools for successful clinical translation," adds Prof. Dr. Dr. Christine Happle, also co-spokesperson. Further information can be found here: www.mhh.de/dekanat-akademische-karriereentwicklung/nextgeneration

Developing new active substances with immune cells

PROF. LACHMANN RECEIVES 2.5 MILLION EUROS FOR FRAUNHOFER ATTRACT GROUP

Prof. Lachmann uses novel reactor vessels that can produce human immune cells on a scalable scale.

Prof. Lachmann's RESIST project is dedicated to alternative therapies against bacterial infections of the lower respiratory tract; in particular, he is investigating the influence of macrophages on the infections. His team has already succeeded in producing these immune cells in scalable systems - i.e. from small scale in the laboratory to industrial use.

The RESIST professor and research group leader at the MHH Clinic for Paediatric Pneumology, Allergology and Neonatology also wants to use these standardised immune cells to test the efficacy and safety of drugs. For this project, he is building the project "IMMUNITY - Designer Cells: New Immune Cell Platforms for Health Research", which is supported by the Fraunhofer-Gesellschaft's Attract funding programme with 2.5 million euros for five years.

The Attract working group is based at the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM.

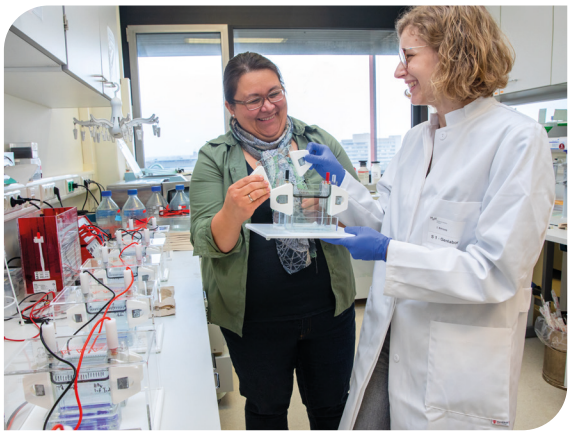
To produce the macrophages, Prof. Lachmann's team uses the properties of induced pluripotent stem cells (iPSC) - biotechnologically "reprogrammed" cells with the property of being able to divide indefinitely and develop into any desired body cell. "This method of standardised production of immune cells from iPSC is a great asset for the research and evaluation of drug candidates because we can test their efficacy and safety directly on the human targets," says the scientist.

The potential of such designer immune cells is huge: for example, they can be genetically modified to light up when they detect impurities in drugs. Up to now, these have been very difficult to detect. Artificial skin tissue, on which cosmetics are already being tested today, could - enriched with immune cells - reproduce the reactions of a human organism even better. It would also be conceivable to test the air quality with such cells, because when we breathe in, it is macrophages and other immune cells that react first to pollutants in the air. It is important to Prof. Lachmann that his research finds its way from the laboratory to the clinic. "An idea only becomes an innovation when it gets into application."

Successful **at RISE**

PhD student Ilka Simons from Prof. Schreiner's research group has been successful at RISE Germany – a programme through which the German Academic Exchange Service (DAAD) arranges research internships for North American, British and Irish undergraduate students at universities and non-university research institutions in Germany. Now, in May, student Raea Michie from Trinity College, Dublin, Ireland, will support Ilka Simons as an intern for two and a half months in the experimental work of her doctorate in Hannover.

Ilka Simons' doctoral thesis is dedicated to adenovirus infection, which is divided into an early and a late phase. The early phase extends to the reprogramming of the cell for the purposes of the viruses, the late phase ends with the production of the virus proteins by the cell. "I am interested in when and why the change occurs. Because if the transition from the early to the late phase could be prevented, the viruses would no longer be able to replicate," she says.

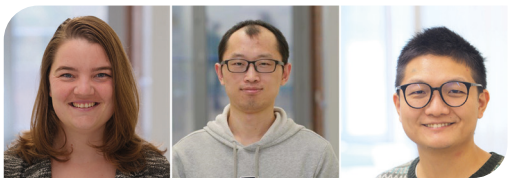


Prof. Schreiner (on the left) and Ilka Simons in the laboratory of the MHH Institute of Virology, with a gel electrophoresis chamber. They use this to make key proteins of the adenovirus infection visible.

WHAT LEADS TO SEVERE **COVID-19 DISEASES?**

TEAM ANALYSES GENETIC AND EPIGENETIC REGULATORS

The team examined individual immune cells from the blood of COVID-19 patients.



The first authors: Dr. Valerie Koeken, Dr. Zhenhua Zhang and Dr. Bowen Zhang (from left).

Infection with SARS-CoV-2 leads to severe disease in some people, whereas others do not get ill or only experience mild disease. But why is this the case? Unfortunately, we do not know exactly. We do know that an overactive innate immune system causes severe COVID-19 disease, but it is unclear how this is regulated.

Prof. Dr. Yang Li's team, which includes numerous other RESIST researchers, has come a step closer to answering this question. They addressed the question of to what extent the course of disease is genetically or epigenetically regulated.

The team was able to identify underlying regulators of the malfunction of the innate immune system in COVID-19 patients and confirm that certain already known genetic risk loci play a role in the development of COVID-19 disease. The results have been published in the journal Cell Genomics. First authors on this publication are Dr. Valerie Koeken together with Dr. Bowen Zhang and Dr. Zhenhua Zhang.

For this study, the team examined individual immune cells from the blood of COVID-19 patients using single-cell multiomics analysis. This technique can be used to simultaneously assess how cells are being regulated and how they are functioning. For this purpose, both the genetic material of the cells is examined and whether certain parts of the genome are 'switched on' (epigenetics) and if genes are transcribed into ribonucleic acid molecules are analysed.

The research team conducted the study at the Centre for Individualised Infection Medicine (CiiM).

In a specific type of white blood cells (monocytes), which are overactivated in severe COVID-19 disease, they were able to identify how altered accessibility to chromatin is regulating gene expression and which transcription factors are steering these dysfunctional monocytes. In addition, they were able to identify how a specific genetic variant is contributing to both a higher viral load and an increased risk of needing hospitalisation for COVID-19. This enabled them to identify one of the factors driving increased susceptibility of severe disease in certain individuals. "Overall, our study highlights the multiple genetic and epigenetic regulators that contribute to COVID-19," summarises Prof. Li.

Research **with change**

One of the first doctoral theses produced in a RESIST project is that of Matthias Bruhn; he defended his work at the end of January 2023. The course was turbulent. At the beginning, he had focused on hepatitis B viruses (HBV). But that changed.

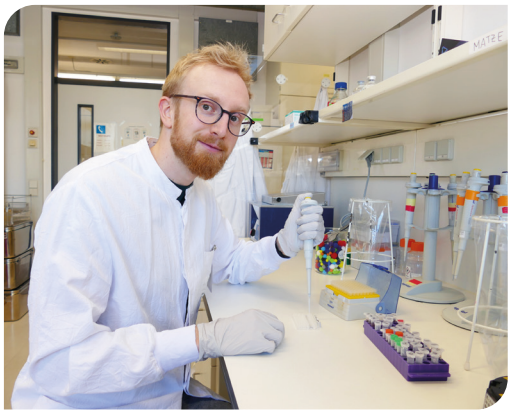
THE CORONA PANDEMIC ALSO TURNED ONE OF THE FIRST DOCTORAL THESES PRODUCED IN RESIST ON ITS HEAD

Why do protective antibodies not develop in about five percent of HBV vaccinees? To find an answer to this question, Matthias Bruhn began his doctoral thesis. Together with Dr. Annett Ziegler, he researched at TWINCORE in the team of the immune response project B9 – supervised by Prof. Kalinke and Prof. Cornberg. They already knew that various genetic components of the immune system play a role in the non-response to vacci-

nation. For example, they knew that certain so-called HLA alleles make it more likely that the vaccination will not work. "I was also able to confirm this fact again in my work," says the researcher. "In addition, we were able to gather evidence that the enzyme TGM2 is important for the immune system to recognise and respond to the vaccine." In perspective, this finding makes it possible to improve vaccinations against HBV.

Matthias Bruhn would have continued to search for reasons for non-response to HBV vaccination. But due to the Corona pandemic, hardly any test persons could be recruited and he lacked samples. To make a virtue out of this necessity, he devoted himself from then on to SARS-CoV-2: "We developed a technique with which we could isolate the very few B cells that produced SARS-CoV-2-neutralising antibodies from blood samples of convalescents," he reported. Using single-cell sequencing, the team was able to find out the exact blueprint of these B cells and produce the antibodies themselves. The best of them were intended as a therapeutic and preventive option. Vaccines did not exist at that time.

But that changed: vaccines were developed and new coronavirus variants emerged against which the antibodies produced were not effective. Which antibodies could protect against as many virus variants as possible? This was now the pressing question. "Knowing that B cells insert mutations into the antibody genes for months, causing the antibodies to mature and work better and better, we developed a new technique to find these more mature antibodies," Matthias Bruhn reports. For people who cannot be vaccinated, for example immunosuppressed patients, this step towards a new therapy option is of great value.



Dr. Bruhn at his laboratory workstation.

Keeping an eye on the *Aspergillus* biofilm: Prof. Routier (right) and her research assistant Patricia Zarnovican

How to get rid of a sticky molecule

INFECTIONS WITH THE FUNGUS *ASPERGILLUS FUMIGATUS* ARE DIFFICULT TO COMBAT

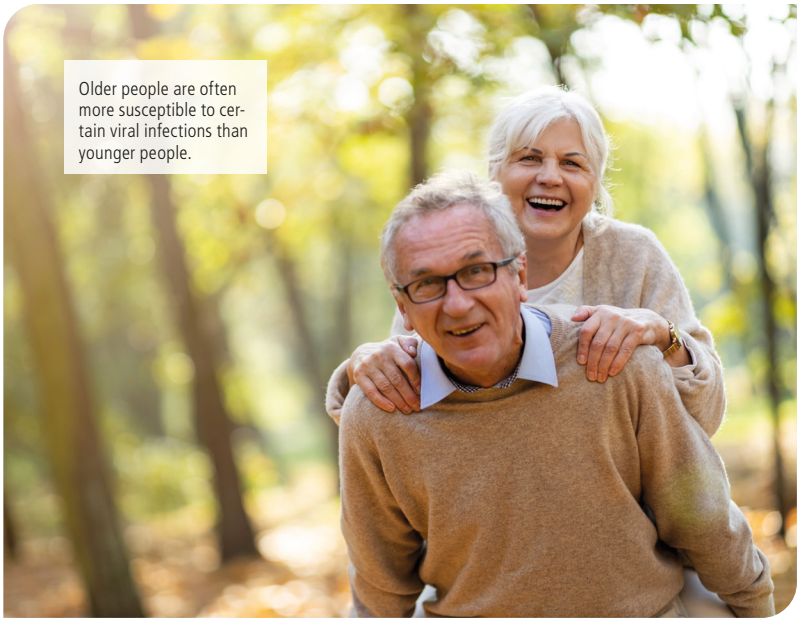
When immunocompromised people breathe in spores of the fungus *Aspergillus fumigatus*, aspergillosis can develop in the lungs. The infection is particularly difficult to treat – in part because the fungus surrounds itself with a biofilm that allows the fungus to attach to tissue and protects from attacks by the immune system and from antifungal drugs. A team led by Prof. Dr. Françoise Routier, MHH Institute for Clinical Biochemistry, has now found a drug from cancer therapy that prevents the formation of Aspergillus biofilm. The study was carried out with the support of RESIST and has been published in the International Journal of Molecular Sciences.

"One of the main components of this biofilm is a sugar molecule that the fungus itself produces and exports into its immediate environment," explains Prof. Routier. There, it is chemically modified by an enzyme called deacetylase Agd3 and becomes sticky.

The biochemist has now found a substance that inhibits the enzyme Agd3 and thus prevents the formation of the biofilm: Imatinib, which is used in cancer therapy. In cell culture, it was able to significantly reduce the *Aspergillus* biofilm and studies on larvae of the wax moth *Galleria mellonella* also confirmed the effect.

Before imatinib can be used against biofilms in humans with aspergillosis, its efficacy as an Agd3 inhibitor would need to be enhanced. "A potent Agd3 inhibitor would help the immune system and boost the efficacy of antifungals. This give us great hope for the development new combinatorial therapy against the fungus," says Prof. Routier.

RESIST-Cohort: Important milestones reached



Older people are often more susceptible to certain viral infections than younger people.

Shingles, influenza, SARS-CoV-2 – Why are older people often more severely affected or even more susceptible to certain viral infections than younger people? How efficiently does the ageing immune system fight off pathogens and what influence do lifestyle, diet and microbiome have on this? In order to be able to answer these questions and to clarify further connections between viral infectious diseases and age, a RESIST team established the "Senior Individuals Cohort" at the end of 2019. As planned, a total of 650 mainly elderly citizens from Hanover have since been included in this cohort and, despite the Corona pandemic, half of the 350 planned follow-up visits have already been carried out.

The first insights were provided by the extensive interviews that were conducted with the participants – on general living conditions, lifestyle and dietary habits as well as on illnesses, vaccinations and medication intake. For example, 17 percent of the test persons stated that they had already suffered from herpes zoster (shingles); 35 percent had suffered from one to two, five percent even three or more upper respiratory tract infections in the period of one year before recruitment and more than 40 percent answered the question about an allergy in the affirmative.

In addition, the results of the genetic analyses of all participants are already available and the composition of the immune cells and the microbiome are currently being analysed. "Currently, we are investigating a subset of samples (serum, plasma, immune cells) with a focus on susceptibility to infection to SARS-CoV-2 as part of the COVID-19 Research Network Lower Saxony (COFONI)," says Dr. Lennart Rösner, a scientist at the MHH Department of Dermatology, Allergology and Venereology, who is in charge of the cohort's daily laboratory processes.

For the analysis of the biomaterials, financial resources from various sources were able to be used to evaluate initial data. Based on these evaluations, further funding is currently being obtained in order to be able to carry out more in-depth planned measurements with the collected biomaterials.

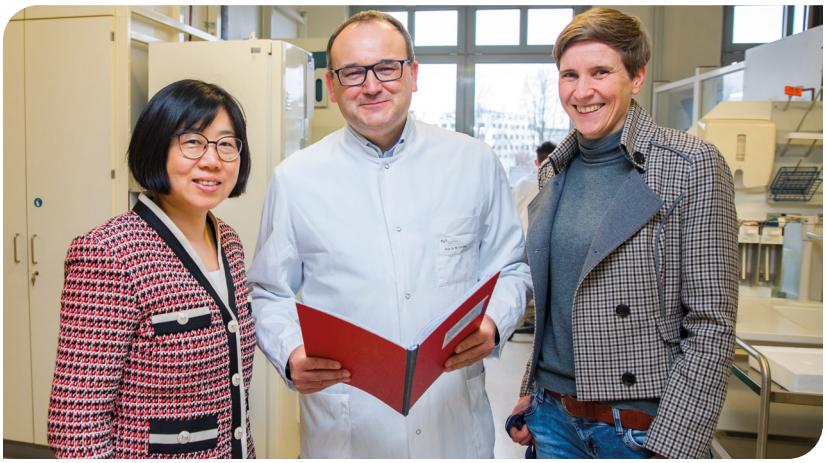
The RESIST cohort represents a central RESIST project in which different RESIST projects participate and contribute different types of data. The data from the healthy participants of the SI cohort can be compared in the next step with relevant data from patients from other cohorts involved in RESIST – with the aim of being able to better understand and treat diseases.

Dr. Castell has taken over the tasks of **Prof. Krause**

The subjects of the RESIST cohort are recruited and interviewed at the HZI Study Centre in Hannover and the samples are also taken there. Until now, Prof. Dr. Gérard Krause has been in charge of this work. Since he moved to the WHO at the beginning of March this year and now works in Geneva, Dr. Stefanie Castell has taken over his tasks. She had previously headed the iAR project, an intensified infection sub-cohort of the RESIST cohort.

Dr. Castell studied medicine in Germany and the UK and completed her training as a specialist in physical and rehabilitative medicine in 2009. Following her clinical work, she studied epidemiology in Berlin and worked in the field of tuberculosis. Since 2012, she has worked as an epidemiologist at the HZI in Braunschweig, since 2016 as deputy head of the Department of Epidemiology. She co-founded the international PhD programme "Epidemiology" at the MHH and the HZI and is Principal Investigator in the German National Cohort (NAKO). Her research focuses on transient common infections, climate-sensitive infectious diseases, self-collection of biospecimens and digital epidemiology.

Her research focus at RESIST is digital epidemiology. Together with her team, she wants to research acute transient infections such as influenza and the associated risk factors. To this end, she wants to use the specially developed "Prospective Monitoring and Management App" app (PIA) in population-based long-term cohorts and thus, for example, search for immunological markers and patterns of microbiota composition as risk factors or predictors of susceptibility to infection (www.info-pia.de).



They are committed to personalised medicine (from left): Prof. Li, Prof. Cornberg and Dr. Debarry.

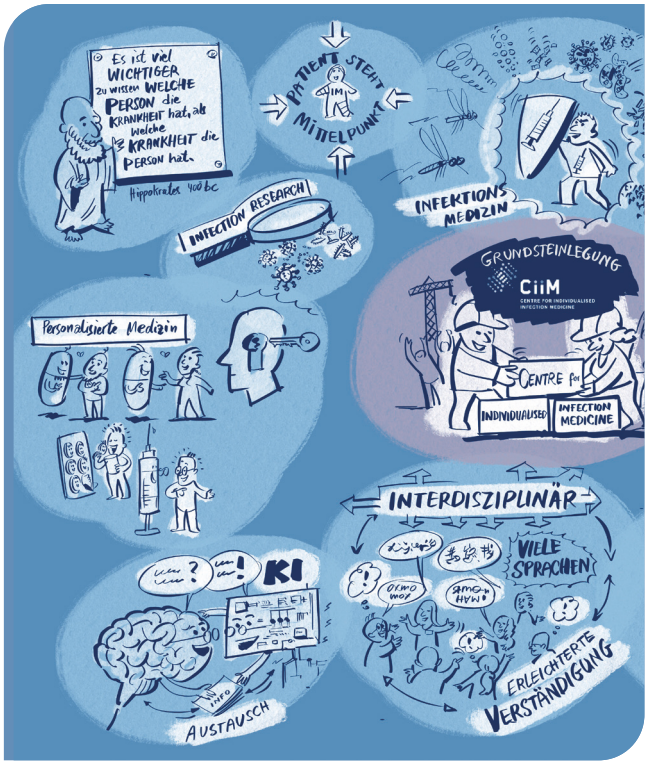
Treat more individually: **The CiiM**

To be able to treat people with infectious diseases even better on an individual basis – that is the goal of the Centre for Individualised Infection Medicine (CiiM), which is headed by Prof. Cornberg and Prof. Li. With its own building now under construction, the interactions between CiiM and RESIST will also increase.

The CiiM researchers are looking for biomarkers that reveal susceptibility to diseases or good response to vaccinations, explore individual disease courses and search for new immune and cell therapies. In doing so, they build on research results that have been developed at the site and expand them in the direction of application.

So far, individualised medicine has been used in particular for cancer, but there are also numerous applications in infection medicine. In order to expand the spectrum of individualised infection medicine, the CiiM researchers are devoting themselves to the disease hepatitis B, for example. This is being done in Prof. Cornberg's research group "Immunology of Liver Infections", which is already directly assigned to CiiM, as are the groups of Prof. Li and Prof. Xu, both dedicated to bioinformatics. The work of these groups illustrates the great role that the analysis of comprehensive patient data plays in relation to individualised medicine.

Currently, the CiiM team consists of about 50 researchers who still work at the MHH and the Braunschweig HZI. When the move to the new CiiM building is imminent, this first institute in Europe to research infectious diseases from a personalised perspective will grow to around 150 people. "For them, the new building plays a key role – and thus also for the entire topic of individualised infection medicine," says CiiM coordinator Dr. Debarry. CiiM perpetuates the topic of individualised medicine and also plays an important role for RESIST: "Our interactions will strengthen, which will lead to mutual benefits and create important synergies," describes Prof. Schulz.



Impressum

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RESIST supports LISA Summer School

Are you interested in infection and immunology? Then the "Lower Saxony International Summer Academy in Infection and Immunology (LISA)" is just the thing for you! The academy is aimed at young students of life sciences and medicine (Bachelor's / Master's) from all over the world who wish to do a doctorate in immunology or infection research. It includes lectures where lecturers present their scientific work and participation in practical demonstrations and laboratory rotations. LISA will take place for the twelfth time this year – from 27 August to 15 September 2023.

Up to 40 young researchers can participate in the programme, which is significantly supported by RESIST this year. The content of LISA has also been adapted in line with the focus topics of the Cluster of Excellence and includes current topics in immunological and infectiological research as well as introductions to innovative experimental techniques. It covers basic science and translational aspects as well as new therapeutic approaches. Further information can be found on the internet at www.mhh.de/hbrs/lisa. Applications are still possible until 30 April 2023.

RESIST-Retreat

On 20 and 21 April 2023, the leaders of the RESIST research groups will meet for a retreat at Warberg Castle, which is located near Helmstedt. RESIST projects will be presented and discussed there. The meeting will also serve to prepare the application for the continuation of the cluster from 2026.

Visit from **Glasgow**

As part of the German-Scottish project "Hannover-Glasgow Infection Strategy" (HAGIS), five researchers from the "Glasgow Centre for Virus Research" (CVR) will be visiting Hannover from 23 to 25 May to meet with around ten local HAGIS project leaders from Hannover. Among them will be CVR director Prof. Dr. Massimo Palmarini. The meeting of the international team will focus on the expansion of further cooperation opportunities, including the planning of a joint research training group.

HAGIS was established in 2021 by RESIST and CVR to conduct long-term research together, complementing each other and thus advancing the development of new therapies for infectious diseases, as well as enabling doctoral students to benefit from the combined research strengths of the two locations. The Ministry of Lower Saxony has supported HAGIS financially for two years.

New concept for the **RESIST-seminars**

The first project round of the RESIST seminar series will end in mid-May. Starting in June, there will be a new concept: The seminars will take place as usual on Thursdays from 5 to 6 p.m. in Lecture Hall Q, but only twice a month. On the first Thursday of each month, an external speaker will give a talk, and on the third Thursday of each month, a RESIST researcher will have the opportunity to present his or her project on a voluntary basis. Please feel free to contact the RESIST office at (0511) 532-4107 or by email RESIST@mh-hannover.de.

Masters's programme: Applications are now open

Between 30 April and 15 July 2023, interested students can apply for the Master's programme in Biomedical Data Science. The German-language programme is aimed at graduates with a Bachelor's degree in biosciences or a degree in veterinary or human medicine. It was developed within the framework of RESIST with significant participation of the Peter L. Reichertz Institute for Medical Informatics. All interested parties are cordially invited to participate in the online information events. They will take place on 11 May 2023 and 13 June 2023, both at 4 pm, and require registration via the following link: www.mhh.de/master-biomeddat/termine. The contact person is the programme coordinator Dr. Melina Celik, telephone: (0511) 532-5700, e-mail master.biomeddat@mh-hannover.de.

Cluster meeting

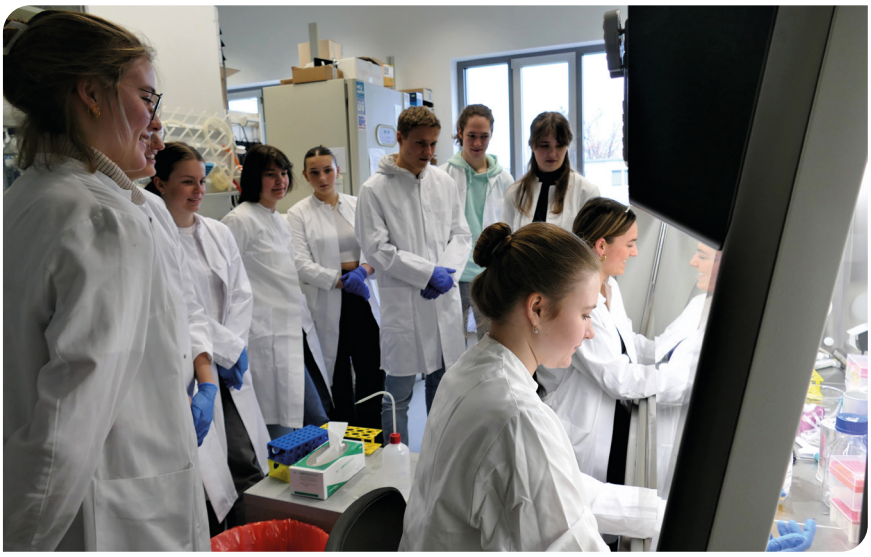
On 22 and 23 June, RESIST board members will meet with board members of the Cluster of Excellence "Balance of the Microverse" from Jena and the Cluster of Excellence "Controlling Microbes to Fight Infections" from Tübingen at Kloster Eberbach, Eltville am Rhein. The aim of the meeting is to network and plan a joint science symposium to be held in 2024.

At a distance: Prof. Förster (left) and Prof. Brinkmann at a festive table.

COVID –
and what happens next?

COVID – and what happens next? Prof. Brinkmann and Prof. Förster summarised the past three years with SARS-CoV-2 and ventured a look into the future on 17 January at Schloss Herrenhausen as part of the Herrenhausen Late event series.

Looking back, they recalled the first warning from Chinese doctor Li Wengliang, who recognised the dangers of COVID-19 pneumonia caused by the new coronavirus variant SARS-CoV-2 as early as 2019. From there, they showed again how quickly the virus sequence was published and the PCR test was produced. They talked about lockdowns, the declaration of the pandemic and vaccine development, and they showed, among other things, what is known today about SARS-CoV-2 and the course of infection. Their presentations were as much about the "dance with the virus" as they were about the success story of vaccinations and mistakes in dealing with the pandemic. "The pandemic is not over yet," said Prof. Brinkmann. The virus will stay with us, she said, and can always develop new strategies to evade our immune system. "We need to do more to be better prepared for the next pandemic." The health system needs to be reformed, vaccines continuously developed and air hygiene improved – she listed as examples of what needs to be done. "Currently, there is good immune protection in the population," said Prof. Förster. But a second booster vaccination could be recommended by the STIKO for everyone. That would depend on which variants emerge and how well the vaccines can be adapted to the variants. Some of the approximately 100 members of the audience asked questions afterwards, before the evening came to an end with delicious cocktails.



In a laboratory of the Hans-Borst-Centre: Pupils at UniStem Day.

UniStem **Day 2023**

Put on a labcoat and gloves and off you go: At this year's UniStem Day at the MHH, organised by the team of RESIST-Professor Dr. Nico Lachmann, Dr. Ruth Olmer and Dr. Sylvia Merkert, 33 senior high school students were able to experience stem cell research directly.

In the morning, they learned through lectures how broken hearts can be healed, which path leads to the artificial stem cell niche and how lung diseases in children are treated. Afterwards, the students were able to conduct their own experiments on stem cell research in four different laboratories. The focus was on the liver, the lungs and the blood as well as the topic of gene therapy. For example, they were able to "split" stem cells, i.e. detach them from the nutrient medium and seed them again so that they continue to divide. They were also able to look at the cilia beat of lung epithelial cells and marvel at "beating" heart muscle cells produced from stem cells. The young women and men pipetted to isolate bacterial genes and harvested stem cells to produce cell aggregates that then produce immune cells in cell culture for infection research.

In the afternoon, the focus was on the various career paths that exist in research. The young women and men had the opportunity to get to know the different jobs and career stages in science - even in person. They were able to talk to students, participants in the Voluntary Scientific Year (FWJ), doctoral students and other researchers.

The participants were enthusiastic: "I found it interesting to be allowed to experiment in a real laboratory myself and it was especially exciting to get to know the different professions that exist in the field of research at a university," reports 17-year-old Roz from the eleventh grade at the Luther School. "I really enjoyed the different experiments and especially the direct, personal exchange with the researchers. I definitely want to become a researcher," says 19-year-old Charlie from Burgdorf Grammar School.

On UniStem Day on 10 March 2023, more than 600 research institutions around the world opened their doors to around 40,000 interested high school students to devote an entire day to stem cell research. It took place for the eighth time.

Hannover Medical School was also involved again. The organisers were supported by RESIST, the German Centre for Lung Research (DZL) and the Centre for Regenerative Medicine REBIRTH.

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RESIST – About us

The clinicians and scientists working in the Cluster of Excellence RESIST (Resolving Infection Susceptibility) aim to offer scientific excellence for the people most vulnerable to infections. RESIST researchers work at **Hannover Medical School** (MHH), **TWINCORE** Centre for Experimental and Clinical Infection Research, **Helmholtz Centre for Infection Research** (HZI) in Braunschweig, **Centre for Structural Systems Biology** (CSSB) Hamburg, **Centre for Chronic Immunodeficiency** Freiburg (CCI) and the **University of Veterinary Medicine Hannover**, Foundation (TiHo). The work of the Cluster of Excellence RESIST is funded by the **German Research Foundation** (DFG).